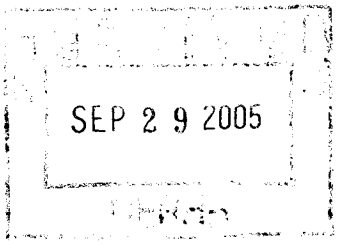
American Chemistry Council

September 28, 2005

Dr. Michael D. Shelby
CERHR Director
CERHR
79 T.W. Alexander Drive
Building 4401, Room 103
Research Triangle Park, NC 27709



Dear Dr. Shelby:

On September 28, 2005, the American Chemistry Council Phthalate Esters Panel (PE Panel) submitted, via email, comments on the August 2005 *Draft Expert Panel Update on the Reproductive and Developmental Toxicity of Di(2-ethylhexyl) Phthalate* (Draft Update). In those comments, we cited several recent studies that were not reviewed in the Draft Update, and stated that we would provide you with hard copies of those studies to facilitate your evaluation of our comments. Enclosed are those hard copies, which comprise 19 studies, as listed below and indicated by asterisks in the References Section of the September 28 comments.

Studies Included With This Letter

1. Anderson W, Castle L, Scotter M, Massey R, Springall C. 2001. A biomarker approach to measuring human dietary exposure to certain phthalate diesters. Food Additives & Contaminants 18(12):1068-174.
2. Barlow NJ, Phillips SL, Wallace DG, Sar M, Gaido KW, and Foster PMD. 2003. Quantitative changes in gene expression in fetal rat testes following exposure to di(n-butyl) phthalate. Toxicol. Sci. 73:431-451.
3. Blowey D, and Warady B. 1998. Neonatal outcome in pregnancies associated with renal replacement therapy. Advances in Renal Replacement Therapy 5:45-52.
4. Chan W, Okun N, and Kjellstran C. 1998. Pregnancy in chronic dialysis: a review and analysis of the literature. Artificial Kidney and Dialysis 21:259-268.
5. Dalgaard M, Nellemann C, Lam HR, Sorensen IK, Ladefoged O. 2001. The acute effects of mono(2-ethylhexyl)phthalate (MEHP) on testes of prepubertal Wistar rats. Toxicol Lett 122:69-79.
6. Fisher JS, Macpherson S, Marchetti N, and Sharpe RM. 2003. Human 'testicular dysgenesis syndrome': a possible model using in-utero exposure of the rat to dibutyl phthalate. Human Reprod. 18:1383-1394.

7. Hack M, Flannery DJ, Schluchter M, Carter L, Borawski E, Klein N. 2002. Outcomes in young adulthood for very-low-birth-weight infants. The New England Journal of Medicine 3:149-198.

8. Ishihara M, Itoh M, Miyamoto K, Suna S, Takeuchi Y, Takenaka I, Jitunari F. 2000. Spermatogenic disturbance induced by di(2-ethylhexyl)phthalate is significantly prevented by treatment with antioxidant vitamins in the rat. Int J Androl 23:85-94.

9. Ito Y, Yokota H, Wang R, Yamanoshita O, Ichihara G, Wang H, Kurata Y, Takagi K, and Nakajima T. 2005. Species differences in the metabolism of di(2-ethylhexyl) phthalate (DEHP) in several organs of mice, rats, and marmosets. Arch Toxicol 79:147-154.

10. Kleymenova E, Swanson C, Boekelheide K, and Gaido KW 2005. Exposure *in utero* to di(n-butyl)phthalate alters the vimentin cytoskeleton of fetal rat Sertoli cells and disrupts Sertoli cell-gonocyte contact. Biol Reprod 73:482-490.

11. Kurata Y, Makinodan F, Okada M, Kawasuso T, David RM, Gans G, Regnier F, and Katoh M. 2003. Blood concentration and tissue distribution of 14C-di(2-ethylhexyl)phthalate (DEHP) in juvenile and adult common marmoset. Toxicologist 72:384.

12. Mylchreest E, Sar M, Wallace DG, and Foster PMD. 2002. Fetal testosterone insufficiency and abnormal proliferation of Leydig cells and gonocytes in rats exposed to di(n-butyl) phthalate. Reprod Toxicol 16:19-28.

13. Ono H, Saito Y, Imai K, Kato M. 2004. Subcellular distribution od Di-(2-ethylhexyl)phthalate in rat testis. J. Toxicol. Sci. 29:113-124.

14. Sharpe RM, Walker M, Millar MR, Atanassova N, Morris K, McKinnell C, Saunders PT, and Fraser HM. 2000. Effect of neonatal gonadotropin-releasing hormone antagonist administration on sertoli cell number and testicular development in the marmoset: comparison with the rat. Biol Reprod 62:1685-93.

15. Reister F, Reister B, Heyl W, Riehl J, Schroder W, Mann W, and Rath W. 1999. Dialysis and pregnancy – A case report and review of the literature. Renal failure 21:5.

16. Toma H, Tanabe K, Tokumoto T, Kobayashi C, and Yagisawa T. 1999. Pregnancy in women receiving renal dialysis or transplantation in Japan: a nationwide survey. Nephrol Dial Transplant 14:1511-1516.

17. Silva MJ, Barr DB, Reidy JA, Kato K, Malek NA, Hodge CC, et al. 2003. Glucuronidation patterns of common urinary and serum monoester phthalate metabolites. Arch Toxicol 77:561-567.

18. Verma RJ, Nair A. 2001. Vitamin E ameliorates aflatoxin-induced biochemical changes in the testis of mice. Asian J Androl 3:305-309.

19. Yu, X., Sidhu, J.S., Hong, S., and Faustman, E.M. (2005). Essential role of extracellular matrix (ECM) overlay in establishing the functional integrity of primary neonatal rat Sertoli cell/gonocyte co-cultures: an improved *in vitro* model for assessment of male reproductive toxicity. Toxicol Sci 84: 378-393.

If you have any questions, or if you need any further information, please call me at (703) 741-5623, email me at Marian_Stanley@americanchemistry.com, or write me at the address on the first page of this letter.

Sincerely yours,

Marian K. Stanley
Senior Director, CHEMSTAR
Manager, Phthalate Esters Panel

Enclosures